INSIGHTS INTO POTENTIAL MECHANISMS OF MERCURY TOXICITY

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ABSTRACT

Mercury (Hg) is a leading concern among the toxic metals addressed in the 1990 Clean Air Act Amendments because of its neurotoxicity. Although Hg poisoning has been recognized for centuries, the biochemical mechanism of its toxicity has remained elusive. Ironically, a contributing factor in how Hg poisons cells may involve its binding with an element that until thirty years ago was known only as a poison itself, selenium (Se). Although in certain regions of the world, soil and water sources can be dangerously high in Se, in other regions Se is hazardously low. Unlike Hg, which is without biological function, small amounts of Se are essential. Living creatures make 20–30 Se-containing proteins (selenoproteins), which are present in varying amounts in all cells of the body. Although the functions of these various selenoenzymes are diverse and in some cases remain unknown, several are known to be active in detoxifying free radicals–dangerous oxygen products generated during normal cellular respiration. If excessive free radicals accumulate, damage or death of the cell can result. While other body tissues have additional enzyme systems available to assist the selenoenzymes in this function, these are less active in brain tissues. Dependence of brain tissues on protection by selenoenzymes may explain why brain tissues are "the first to use and the last to lose" Se.

It has been recognized that providing additional Se prevents death in animals fed otherwise toxic amounts of Hg, but results in accumulation of insoluble mercury selenides. Recent studies of Hg and Se physiology reveal that Se may not simply protect against Hg toxicity, it may be that Hg's toxicity occurs through its impact on selenoprotein synthesis. Animal studies have demonstrated that when too much Hg is in the diet, formation of selenoproteins in fetal brain tissues is reduced. Providing additional dietary Se helps the fetal brain cells to maintain selenoprotein synthesis to overcome this deficit. However, if too much Se is lost to formation of these precipitates, cells could be damaged and perhaps die. Death of neuronal cells during neurodevelopment in the fetus would preclude ensuing generations of cells and impair normal development of essential brain tissues.

Defining the pathophysiology of Hg toxicity appears to be more complex than simply delineating how much Hg was consumed. Instead, the critical question may be, "Was so much Hg consumed and absorbed in brain tissues that it bound up all the free Se available or was there sufficient excess Se present in the cells to support selenoenzyme synthesis?" Since selenoenzyme synthesis can be more easily impaired when cellular selenium reserves are low, the potential contributing effects of low-selenium status in regions noted for mercury toxicity needs careful examination. Sensitivity to Hg-induced neurotoxicity may be the result of the balance of the relative amounts of Hg and Se acting in this delicate biological equation.